RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 78, 83, 86, 87 and 92 are amended herein, and claim 85 has been canceled. Therefore, claims 78-84 and 86-94 are currently pending the application.

Amendments were made to claims 83 and 86 to correct typographical errors. Support for amendments to claim 78, 86, 87, and 92 can be found in the specification, at least, on page 34 lines 7-12 of the specification.

B. Priority

The action notes that, though a statement of priority was included in the application the priority statement failed to expressly define the relationship of the current application to prior applications, and the current status of prior applications. In response the specification has been amended to recite current status of priority documents, and their relation to the present application. In view of these amendments it is respectfully requested that the objection to the application under 37 CFR 1.78(a)(2) and (a)(5) be removed.

C. Specification

The Action objects to the current application for improper sequence disclosure as defined in 37 CFR § 1.821(a)(1) and (a)(2). In response the specification has been amended to include a new sequence identification number, SEQ ID NO:88, and a corresponding reference to the sequence identification number in the text. A substitute sequence listing and computer readable sequence listing as required under 37 C.F.R. § 1.825, accompany this response.

The specification is further objected to for improper demarcation of trademarks. In response the specification has been amended to clearly define trade marks that are used in accordance with the MPEP § 608.01(v).

The specification is further objected to for inclusion of embedded hyperlinks. In response embedded hyper links have been removed where appropriate. In view of the forgoing amendments to the specification, it is respectfully requested that objections to the specification detailed, detailed in the Office Action, be removed.

D. Rejection of Claims Under 35 U.S.C. §112, First Paragraph

1. Written Description

The Action rejects claims 78-94 as failing to comply with the written description requirement stipulated in 35 U.S.C. §112, first paragraph. The Action asserts that the specification does not effectively define a function for polypeptides encoded by the nucleotide sequences of the invention. Further the Action states that without description of a function for these polypeptides it is unpredictable that an agent could be used to inhibit their function. In response claims 78, 86, 87 and 92 have been amended to recite "an agent that binds to a peptide or polypeptide encoded by [the sequences of the invention]." The specification clearly provides written description for an agent that binds to a polypeptide of the invention, for example on page 44 lines 20 to 27 the specification states that:

> It will be appreciated by those of skill in the art that monoclonal or polyclonal antibodies specific for proteins that are preferentially expressed in metastatic or nonmetastatic human prostate, bladder or breast cancer will have utilities in several types of applications. These may include the production of diagnostic kits for use in detecting or diagnosing human prostate, bladder or breast cancer. An alternative use would be to link such antibodies to therapeutic agents,

such as chemotherapeutic agents, followed by administration to individuals with prostate, bladder or breast cancer, thereby selectively targeting the prostate, bladder or breast cancer cells for destruction.

Thus, it is clear that the specification has adequate written description for agents that bind to the polypeptides of the invention and could used to target prostate, bladder and breast cancer cells. Additionally, the specification provides examples of agents that bind to the polypeptides of the invention. Described in the specification is an antibody that was made to UC 28 (encoded by the nucleotide sequence of SEQ ID NOs: 3, 83 and 85). On page 117 lines 4 through 12 state:

> A first generation polyclonal antibody has been produced in rabbits using a KLH conjugated synthetic peptide (21 amino acids). The peptide, of sequence listed below, was chosen for antigenicity by a computer software program (DNASTAR™, Madison, WI).
>
> RKKEKVKRSQKATEFIDYSIE SEQ ID NO:56
>
> The synthetic peptide was conjugated to KLH by standard techniques and injected into two rabbits, with bleeding started at ten weeks. The antibody was peptide affinity purified and then tested in prostate cancer cell lines, and breast and prostate cancer tissue, confirming the localization of the UC 28 protein to epithelial cells, mainly on the cell membrane.

Thus, written description is provided for a species of the claimed agents, and it would be very clear to one of skill in the art that the inventors were in possession of the invention at the time of filing.

It is well established that the patentee need not describe every embodiment on which the claim reads. According to the Federal Circuit, "[i]t is well-established that a patent applicant is entitled to claim his invention generically, when he describes it sufficiently to meet the requirements of section 112." *Amgen v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991); *see also Utter v. Hiraga*, 856 F.2d 993, 998, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) ("A specification may, within the meaning of 35 U.S.C. §112,

paragraph 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.").

The written description requirement has been extensively addressed by the Federal Circuit. In particular, the Federal Circuit has stated that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.'" *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ 2d 1227, 1232 (Fed. Cir. 2000). The Federal Circuit has also noted that "[if] a person or ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met." *In re Alton*, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

Therefore, in view of the forgoing amendments and arguments it is clear that the specification provides adequate written description for the claimed invention, and the Examiner is respectfully requested to withdraw this rejection.

2. Enablement

The Action rejects claims 78-94 under 35 U.S.C. §112 first paragraph, as failing to comply with the enablement requirement. The Action reasserts that the specification fails to disclose a function for the polypeptide encoded by the nucleotide sequence of the invention, therefore, an undue amount of experimentation would be required to "determine the function or activity of the protein, secondly to determine whether the function or activity of the protein correlates with the onset or progression of cancer, and if so, the design or discover a compound that inhibits that function or activity." In response and in view of the amendments presented

above applicant asserts that the enablement requirement is met. Design of an agent that binds to polypeptides encoded by the nucleotide sequences of the invention is well known to those of skill in the art and would not require undue experimentation. Point of fact, the specification has extensive description regarding the construction and use of a species of binding agents, namely polyclonal and monoclonal antibodies, see the section entitled "Preparation of Antibodies Specific for Encoded Proteins" beginning on page 31. Furthermore the specification describes an antibody that was made to the polypeptide encoded by SEQ ID NOs: 3, 83 and 85 (see excerpt above). Furthermore it is pointed out, that effective targeting of cancer cells with a binding agent of the invention does not require determining "the function of the protein" whether "the function correlates with the onset of cancer" or the "discovery of a compound that inhibits the function of the protein".

Additionally, the Action cites Jain and Curti as evidence that the design of new anti-cancer drugs is a "burdensome task" and would require an undue amount of experimentation. However, Applicants assert that use of anti-cancer agents of the invention is not a "burdensome task." For example, in certain embodiments of the invention, binding agents may be conjugated to radionuclides or to chemotherapeutic agents. Both radionuclides and chemotherapeutics are widely used in the treatment of cancer and conjugation to agents of the invention may increase their efficacy or reduce toxicity to healthy tissue. Thus, there would be no requirement for the kind of protracted analyses that the Action indicates would be necessary in order to practice the invention. In fact binding agents that target cancer cells, such as those of the current invention have been used in clinical trials. Carrol, 2004 (Exhibit A) report use of a yttrium-90 labeled monoclonal antibody targets a membrane protein on prostate cancer cells. Results from this study indicated that the antibodies labeled with the radionuclide had "Acceptable toxicity,

excellent targeting of known sites of PC metastases, and biologic activity in patients". Thus, Carroll indicates that agents for the treatment of cancer such as those of the invention are known to be effective for cancer therapy, and even for the treatment of solid tumors. As detailed above the specification provides enabling written description that would allow a person of normal skill in the art to apply the invention for the treatment of cancer without undue experimentation.

In further arguments the Action states that An *et al.* teaches that the polypeptide encoded by SEQ ID NOs: 3, 83 and 85, designated therein as UROC 28, "is not expressed at the surface of cells" citing that immunohistochemical analysis revealed that the protein localized primarily to the nucleus and/or the cytoplasm. The action goes on to cite Vitetta and Bodey as evidence that immunological targeting of cancer cells may be inefficient and that in any case targeting requires that the targeted molecule be expressed on the surface cancer cells. In response, Applicants note that studies described in the specification on page 177 lines 10-14 indicated that the peptide encoded by SEQ ID NOs: 3, 83 and 85 was found on the cell membrane. As further evidence Applicants respectfully submit a declaration of Dr. Veltri (Exhibit B). The declaration was made with respect to a co-pending application but is believed to be relevant here as proof that UC28 (encoded by SEQ ID NOs: 3, 83 and 85) is expressed on the membrane of cancer cells. Therefore, one of skill in the art would expect for an agent that binds to polypeptide sequence encoded by SEQ ID NOs: 3, 83 and 85 to target cancer cells that over express these proteins.

The Action further indicates that the specification teaches that mRNAs corresponding to the sequences of the invention are overexpressed in cancer cells, however, that it does not teach that the polypeptide encoded by these RNAs are overexpressed *per se* and therefore, a method for treating cancer by targeting cells over expressing these polypeptides lacks enablement. Applicants respectfully traverse, because it is demonstrated in the specification that, for instance,

UC 28 mRNA is overexpressed in breast cancer cells (FIG. 15), 4 out 5 bladder cancer cell lines (FIG. 16) and is hormone inducible in prostate in a prostate cancer cell line (FIG. 17). While overexpression of the mRNAs in one cell line might result from random mutation during cancer development, overexpression in a wide range of cells would suggest to one of skill in the art that overexpression of the polypeptide was in fact advantageous to the cancer cell. Thus, the demonstration that a variety of cells over express the sequences of the invention implicitly indicates corresponding polypeptide overexpression. Additionally, An *et al.,* directly show that UC 28 protein (UROC 28) is overexpressed in prostate and breast cancer cells. Therefore, it is clear to one of skill in the art that the specification does teach that UC 28 protein is over expressed in the cancer cells recited in the claims, thus enabling a method of treating cancer that targets cells expressing UC 28.

Finally it is asserted that in some forms of cancer polynucleotides of the invention are not over expressed (*e.g.* colon and lung caner). Thus, the action rejects claims directed to treatment of cancer, in general. In response applicant notes that the current claims recite treatment of breast cancer, bladder cancer or prostate cancer, therefore this rejection is thought moot.

In view of the forgoing amendments and arguments the rejection of claims 78-94 under 35 U.S.C. §112, is thought to be moot and the Examiner is respectfully asked to withdraw the rejection.

E. Double Patenting

The Action provisionally rejects claims 78-94 under the judicially created doctrine of obviousness type double patenting over claims 1-38 and 65-72 of Application No.09/966,762. In response, Applicants note that, if required, a terminal disclaimer over will be submitted upon an

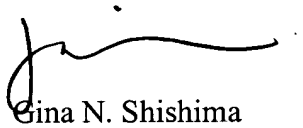
indication that the claims are otherwise allowable. Removal of the rejections is thus respectfully requested.

F. Conclusion

This is submitted to be a complete response to the referenced Office Action. In conclusion, Applicant submits that, in light of the foregoing remarks, the present case is in condition for allowance and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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